

Spiral Molecular Structures  
the Basis of Life.

Carl E. Grafft.

QH  
335  
K 842  
ed. 2



577.012

K 85<sub>6</sub><sub>2</sub>

S P I R A L   M O L E C U L A R   S T R U C T U R E S  
T H E   B A S I S   O F   L I F E.

(Second Edition)

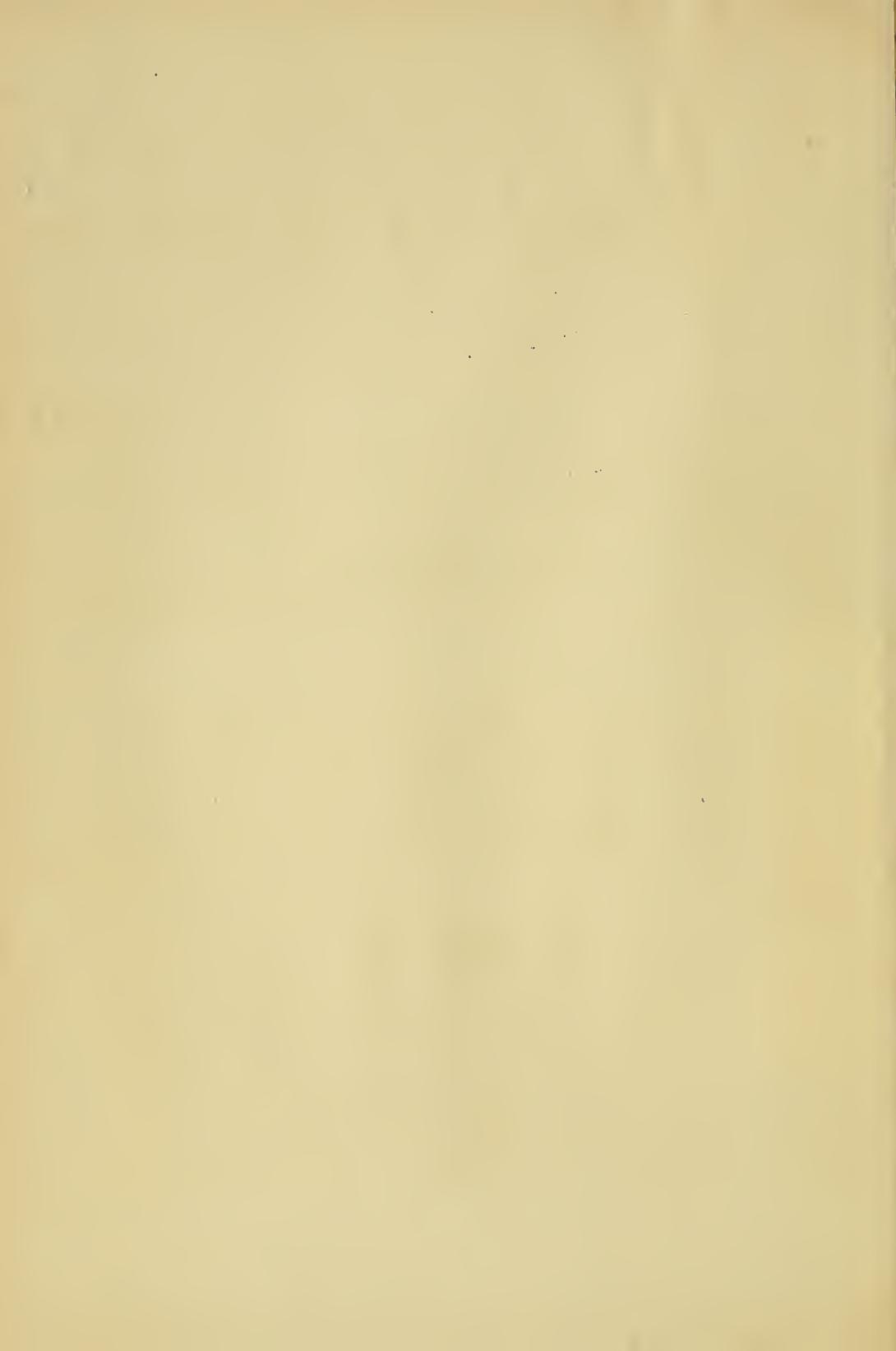
by

Carl F. Krafft,  
Washington., D. C.

1928

MBL/WHOI





1.

S P I R A L   M O L E C U L A R   S T R U C T U R E S  
T H E   B A S I S   O F   L I F E .

Introduction.

There are certain biological processes such as growth, variation, and reproduction, which are exhibited by every living organism, regardless of its rank in the plant or animal kingdom. These processes establish in nature a sharp line of demarcation between living and non-living things, since none of the phenomena of physics or chemistry exhibit anything that is similar or analogous to these fundamental life processes.

Biological growth involves not only the accretion of tissue-building material, but also many remarkable chemical transformations which take place during metabolism, as well as the development, in most cases, of highly complex and heterogeneous structures. The nearest approach to this in the inorganic world is the growth of crystals, but crystal growth produces neither the remarkable chemical transformations nor the complex structures which often result from biological growth, not to mention several minor differences such as the polyhedral form of crystals as distinguished from the rounded form of most living organisms, and the hardness of crystals as distinguished from the softness of most living tissues. The differences between crystal growth and biological growth are so manifest that it seems hardly fair to assign them to the same category, and much less to propose the one as an explanation for the other.



Biological variation differs from all inorganic changes and metamorphoses in that the newly acquired structures exert a directing influence upon the future growth of the individual, and are perpetuated by a process of heredity.

Biological reproduction is likewise so dissimilar from any of the other processes of nature that it seems impossible to establish even the remotest analogy, and much less to attempt to explain it on the basis of any of the known phenomena of physics or chemistry.

These fundamental life processes are exhibited just as fully and completely by the simplest bacteria as by the highest plants and animals. All living organisms, notwithstanding their diversity of form and appearance, must possess something in common which gives rise to that peculiar characteristic called "life".

If the fundamental life processes are due primarily to some specific configuration of tissues or membranes, then such configuration would have to occur in every living organism, including the simplest bacteria. We find in nature many structural uniformities which occur more or less extensively among certain species of plants and animals, but these are the result of evolution and will be found to disappear as we go down the scale of plant or animal life. Even the chromosomes which occur in the cells of all higher plants and animals have never been observed in any of the bacteria, and therefore cannot be regarded as the primary and original cause of the fundamental life processes. It would not be justifiable, in the absence of experimental proof, to assume that chromosomes or similar structural complexities exist in bacteria, merely because they have been observed to exist in the cells of the higher plants and animals.



3.

That the fundamental life processes must be due, either wholly or partly, to specific chemical structures is generally admitted, but there is a prevailing opinion that the molecular structures which are necessary for this purpose must be extremely complex. The failure of all previous efforts to devise some type of molecular structure which would function in a manner similar to the fundamental life processes does not, however, prove that the solution of the problem must lie in the direction of extreme complexity. The complex molecular structures of which the higher plants and animals are composed have developed gradually in the course of evolution, and the fact that they are necessary for the proper physiological functioning of the particular organisms in which they now occur does not prove that they were also the original cause of the fundamental life processes in the more primitive organisms from which these higher plants and animals have developed. If extremely complex molecular structures were necessary for life of any sort, then it would be highly improbable that life could ever have originated spontaneously.



The Chemical Basis of Life.

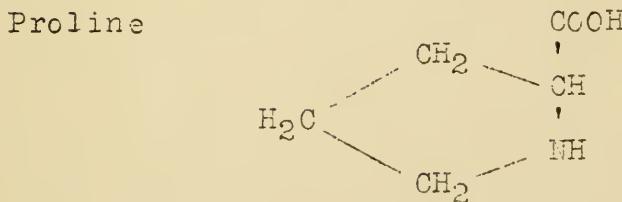
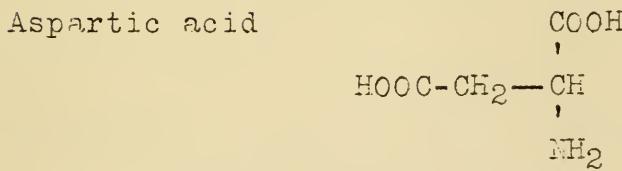
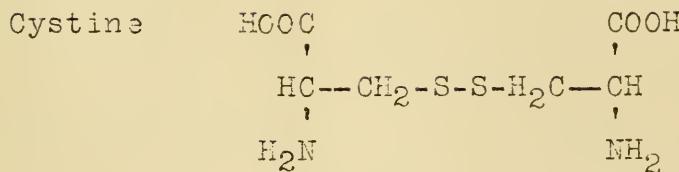
If life cannot be due, primarily, either to specific arrangements of tissues or membranes or to extremely complex molecular structures, then it must be due to some comparatively simple principle of chemistry which has not yet been discovered. To find a clue to this we must investigate the molecular structure of proteins, because these constitute practically all the structural material in the bodies of the simplest unicellular organisms after removal of the water. Although small amounts of fats are also present, yet these do not constitute structural material but appear to be merely the by-products of certain kinds of protein metabolism.

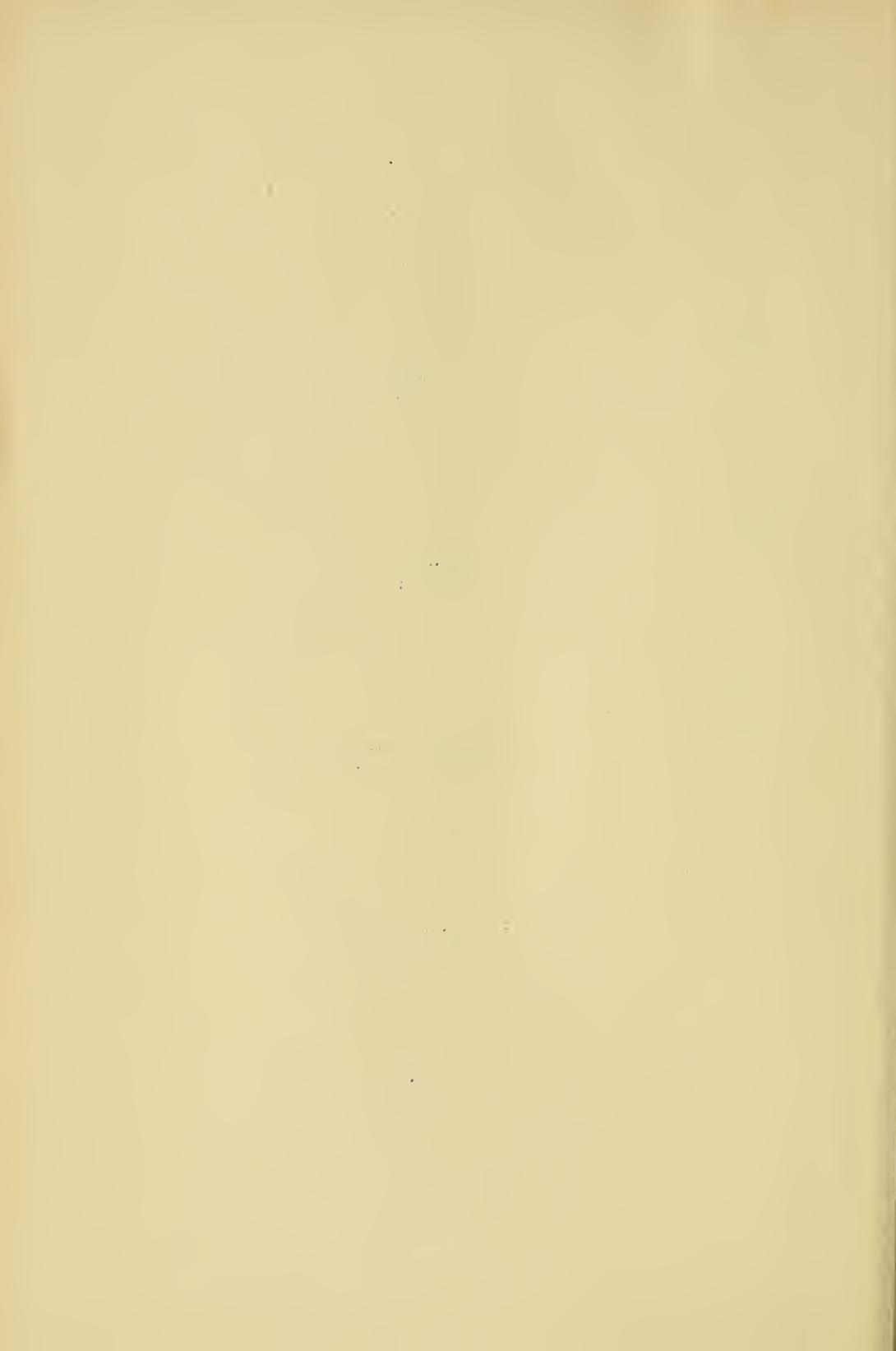
Protein substances, upon hydrolytic decomposition, always yield a mixture of amino acids or their diketopiperazine derivatives. To the alpha carbon atom of these acids there is always attached one amino group and one hydrogen atom, and usually also a more complex group, so that they may be represented generally as follows:



The structural formulae of the more important amino acids are as follows:

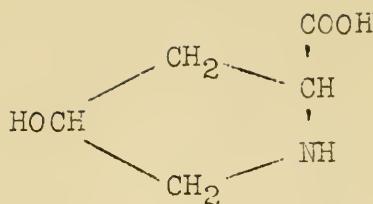






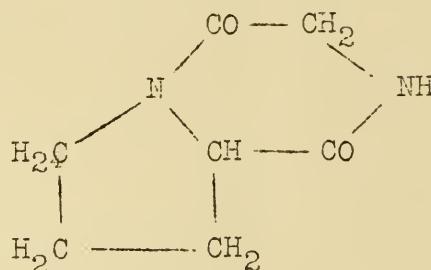
6.

Oxyproline

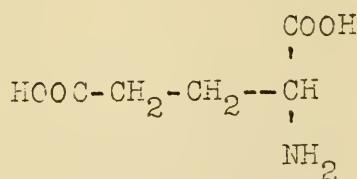


Glycine-proline anhydride

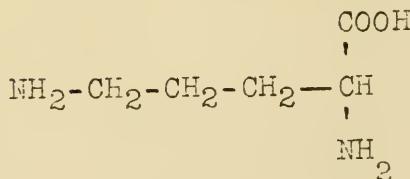
(E. Abderhalden & E. Komn,  
Z. physiol. Chem., 145, 308, 1925.)

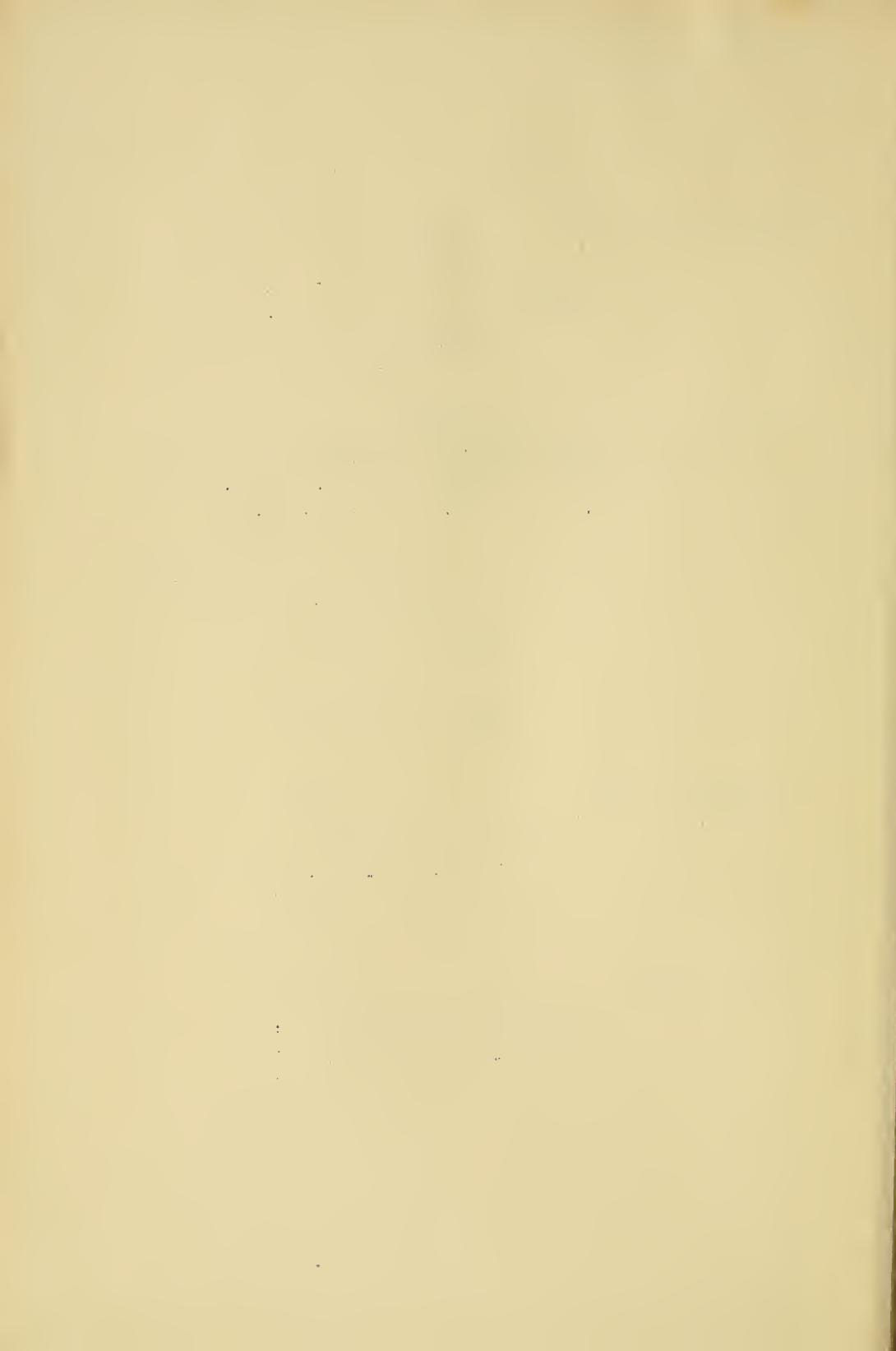


Glutamic acid

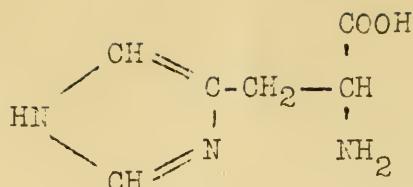


Ornithine

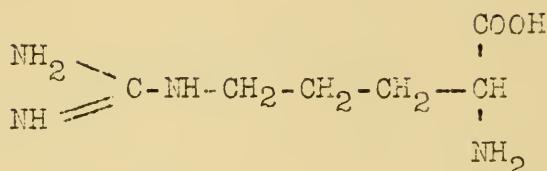




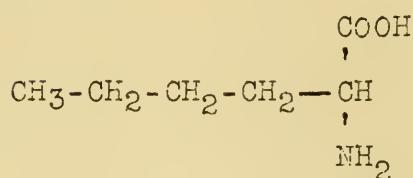
## Histidine



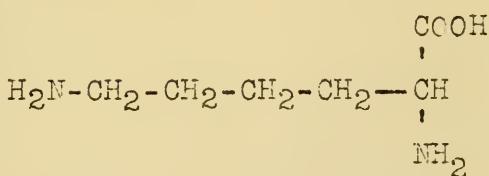
## Arginine



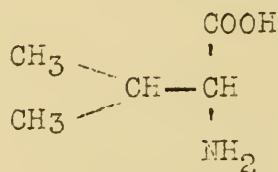
## Caprine



## Lysine

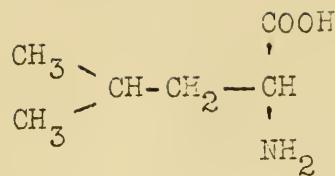


## Valine

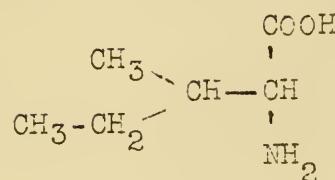




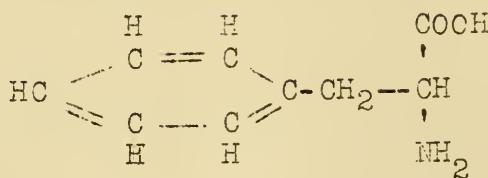
## Leucine



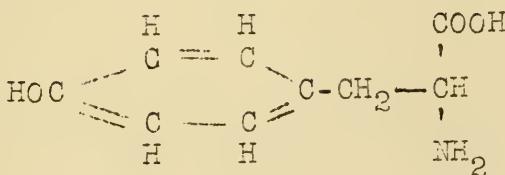
## Iso-leucine



## Phenyl-alanine



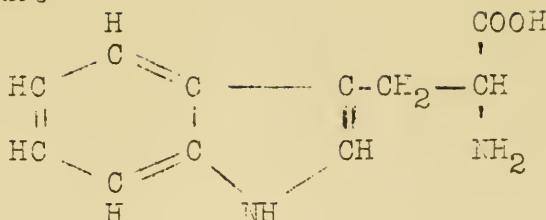
## Tyrosine





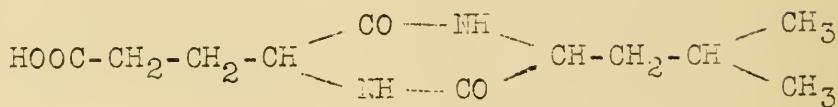
9.

Tryptophane



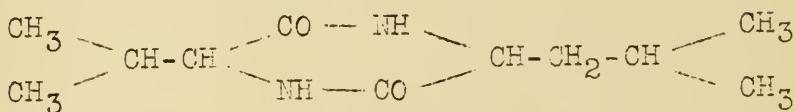
Leucine-glutamic acid anhydride

(P.A. Levine & W.A. Beatty,  
Ber. 59, 2060, 1906.)



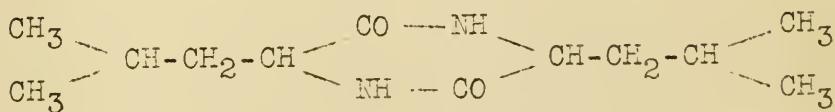
Valyl-leucine

(E. Abderhalden, Z. Physiol. Chem.,  
131, 284, 1923.)



Leucine anhydride

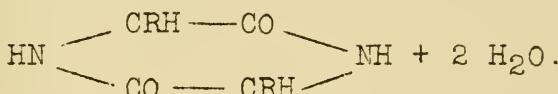
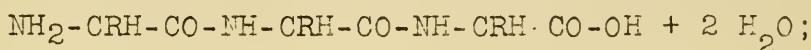
(E. Abderhalden & K. Funk,  
Z. physiol. Chem. 53, 19, 1917.)





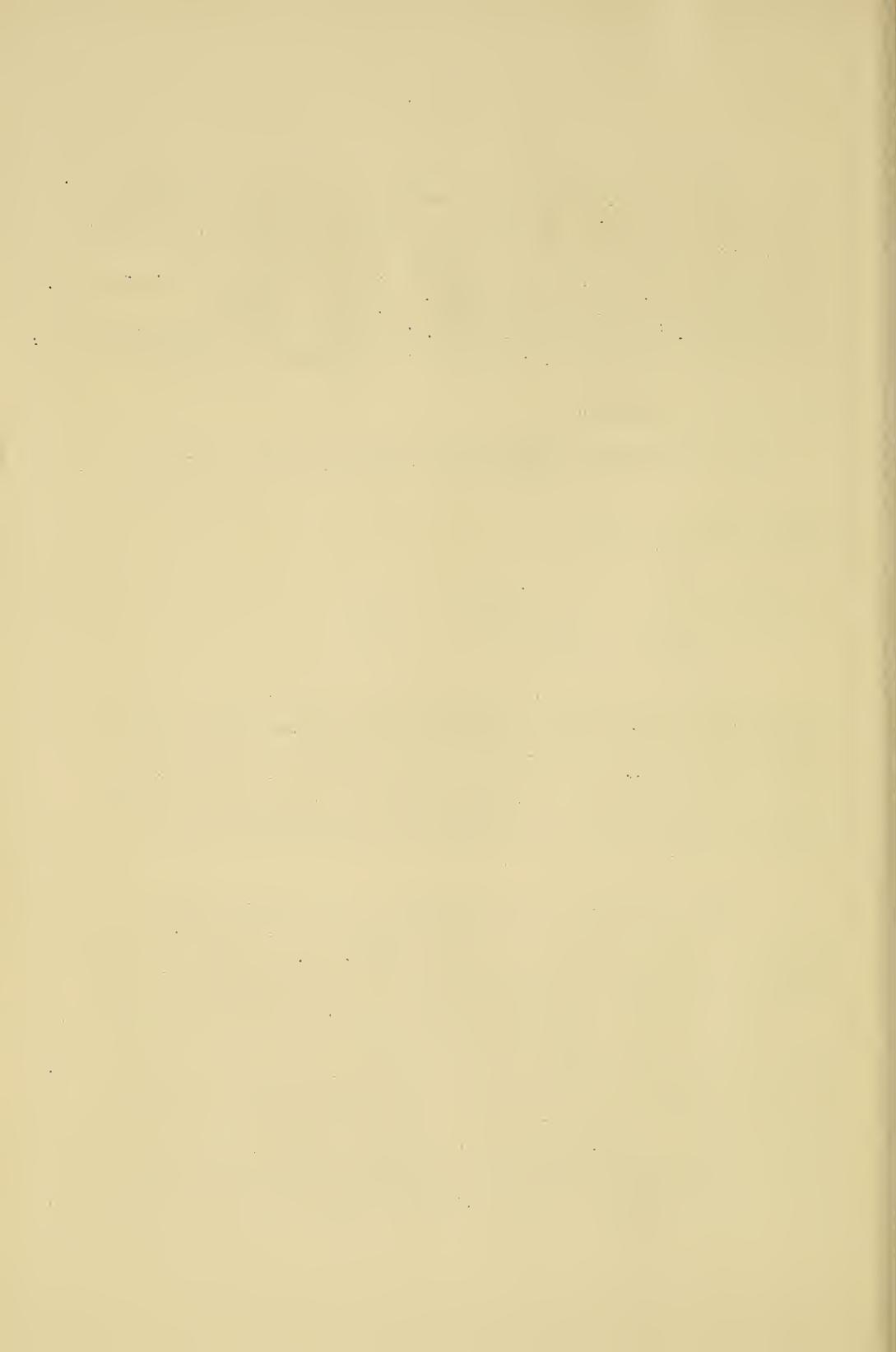
These amino acids will readily condense, with the elimination of water, to form either chain structures known as polypeptides, or ring structures known as diketopiperazines.

(Emil Fischer, Untersuchungen über Aminosäuren, Polypeptide, und Proteine, 1899 - 1906; Plimmer's Chemical Constitution of the Proteins, Monographs on Biochemistry, Longmans, 1912)



Since proteins constitute the principal structure-building food for animals, and upon digestion are decomposed into amino acids, in which form they are assimilated by the tissues, it is generally thought that the phenomenon of growth involves condensation processes of a similar character.

The frequent occurrence of diketopiperazine rings among the disintegration products of proteins seems to indicate that this may be the form in which the alpha amino acid groups occur in nature, but a fatal objection to this theory is that diketopiperazines cannot grow by condensation with additional amino acid molecules. If our purpose is to solve the problem of life, then the biological side of the problem must be given full consideration, and we should have but little patience with any theory which explains only the chemical but not the biological facts.



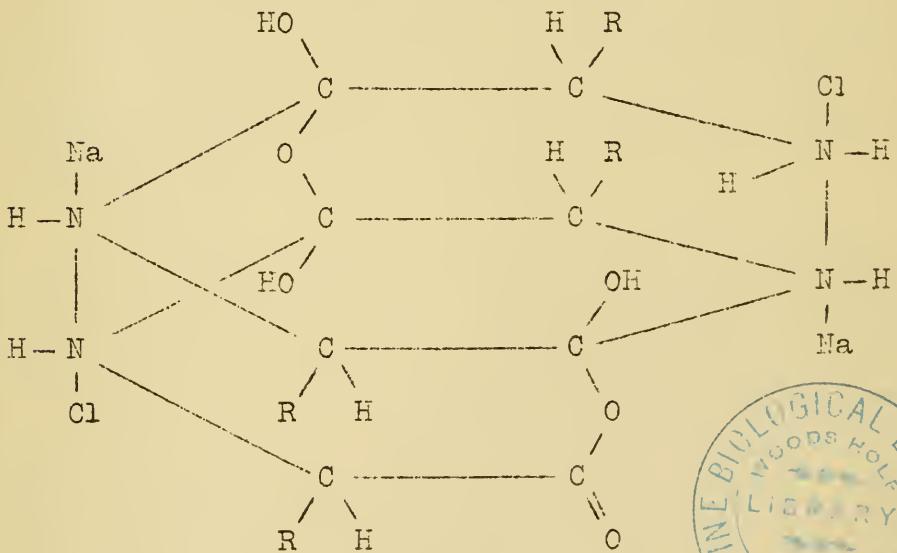
The polypeptide theory teaches that the amino acid groups occur in nature in the form of long polypeptide chains. This theory offers at least a partial explanation for the phenomenon of growth, as well as for structural variation, but in its present form is inadequate in that it does not account for that definite morphology which is possessed by all living organisms, nor for spontaneous division with the transmission of hereditary characteristics to the progeny.

There is, however, another type of structure, namely the helical spiral, which retains the essential characteristics of both the ring and the chain.



Polypeptide Spirals.

If we assume that the valencies of the carbon atom are arranged like the corners of a regular tetrahedron, and that the three valencies of tri-valent nitrogen in amino compounds are about equally distributed around an equatorial circle, (which arrangement appears to be the only one that is consistent with all known chemical facts,) then the polypeptide chain may be coiled around on itself so as to form a helical spiral having substantially the same diameter as the diketopiperazine ring.



A polypeptide spiral in NaCl solution.



The nitrogen atoms will appear in two rows on opposite sides of the spiral, and the complex side chains represented by the R's in the previous equations, as well as the carbonyl groups, will likewise arrange themselves along other diametrically opposite lines. Chemical union will probably take place between the successive nitrogen atoms by virtue of their fourth and fifth valencies, and perhaps also between the successive carbonyl groups in the manner shown. The nitrogen atoms at the ends of the spiral will probably unite with the ions of inorganic salts, the presence of which is necessary for the nourishment of all living organisms. It will be found upon actually constructing this spiral of atomic models that there is ample room for the complex side chains R if the fourth valency of the alpha carbon atom is occupied by hydrogen, but that the presence of more complex groups in this position would make the spiral structure impossible. We find, however, that the decomposition products of proteins always have a hydrogen atom in this position.

It will be observed that the polypeptide spiral in the accompanying diagram has an exposed amino group at one end, and an exposed carbonyl group at the other end. Theoretically it appears that additional amino acid radicals could be added to either end of the spiral, although there may be some at present unknown reason why growth can take place at one end only. A spiral with an exposed amino group at the free end may be designated as positive (+), and one with an exposed carbonyl group at the free end as negative (-). A distinction should also be made between right-handed (r) and left-handed (l) spirals.



The similarity in form and appearance of a polypeptide spiral to a bacillus or a spirillum will be apparent. It should be capable of growing endwise by condensation with additional amino acid radicals, and as long as the spiral form is maintained the structure will possess definite morphology. It must remain permanently right-handed or left-handed which appears to account for the optical activity always exhibited by substances obtained from living organisms. It should be capable, during growth, of acquiring different arrays of side chains upon being nourished with different kinds of amino acids, and thus exhibit the characteristic of variability. It would not, however, upon division, be capable of transmitting to its progeny any permanently inheritable characteristics, and can therefore not be regarded as a complete living organism.



The Linking of Polypeptide Spirals.

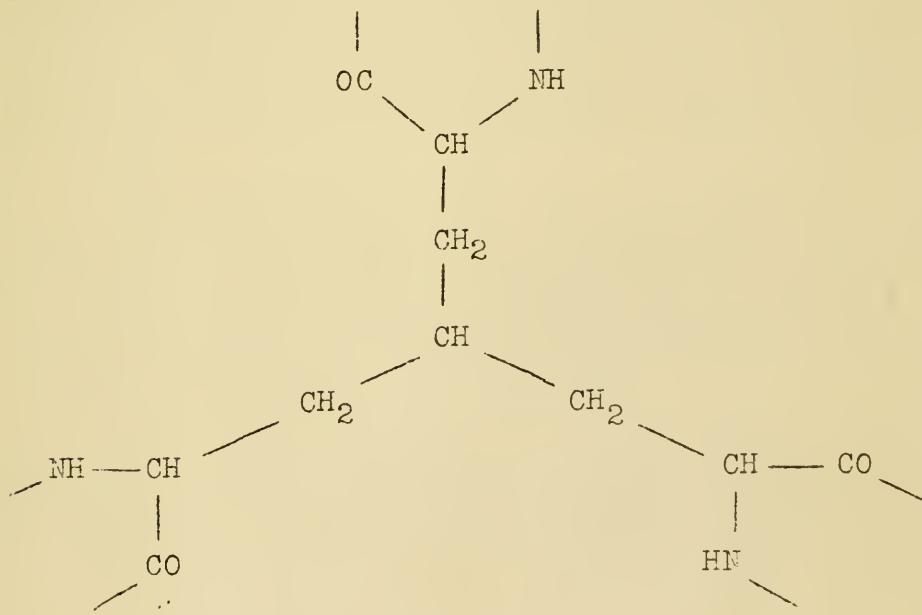
Since the distance between the centers of adjacent carbon atoms is about  $1.54 \times 10^{-8}$  cm, the diameter of a polypeptide spiral, as measured between the centers of the atoms, would be about  $3.1 \times 10^{-8}$  cm. It will therefore require several hundred spirals arranged side by side to produce an organism as large as the smallest visible bacillus, which measures about  $1000 \times 10^{-8}$  cm in diameter. In order that the organism may possess definite individual characteristics, these spirals would have to be coupled together in some permanent manner, but after they are thus coupled together, they will have a tendency to preserve their arrangement throughout growth, and if transverse fission occurs, each portion would have to continue growing according to the original pattern. There will thus be exhibited, in the simplest possible manner, a process of inheritance by which parental characteristics are preserved throughout growth and transmitted to the progeny.

It appears that there are only a limited number of ways in which adjacent spirals can be connected together. The connecting complexes must be comparatively simple, because if more than a certain number of intermediate atoms are present their movements will no longer be definitely coordinated so as to form the required intermediate structures, but will be more or less at random. In order to determine the nature of these connecting complexes, the use of atomic models is recommended, because the problems encountered here are structural rather than dynamic.



The form of connecting complex which occurs most frequently in nature appears to be a triple connection between three adjacent spirals by means of a central carbon atom. The complex groups which are usually attached to the alpha carbon atoms of amino acids are evidently the fragments from such connecting complexes. It appears from a study of protein decomposition products that two types of such triple connections occur in proteins.

Leucine, phenyl-alanine, and tyrosine have a triple junction at the gamma carbon atom, with an intermediate  $-\text{CH}_2-$  group between this triple junction and the  $-\text{CH}-\text{NH}_2-\text{COOH}$  group. The complete triple junction, (assuming it to be the same on all three sides,) together with one-half of each of the three adjacent spirals, will therefore appear somewhat as follows:



A triple junction of the gamma-gamma-gamma type.

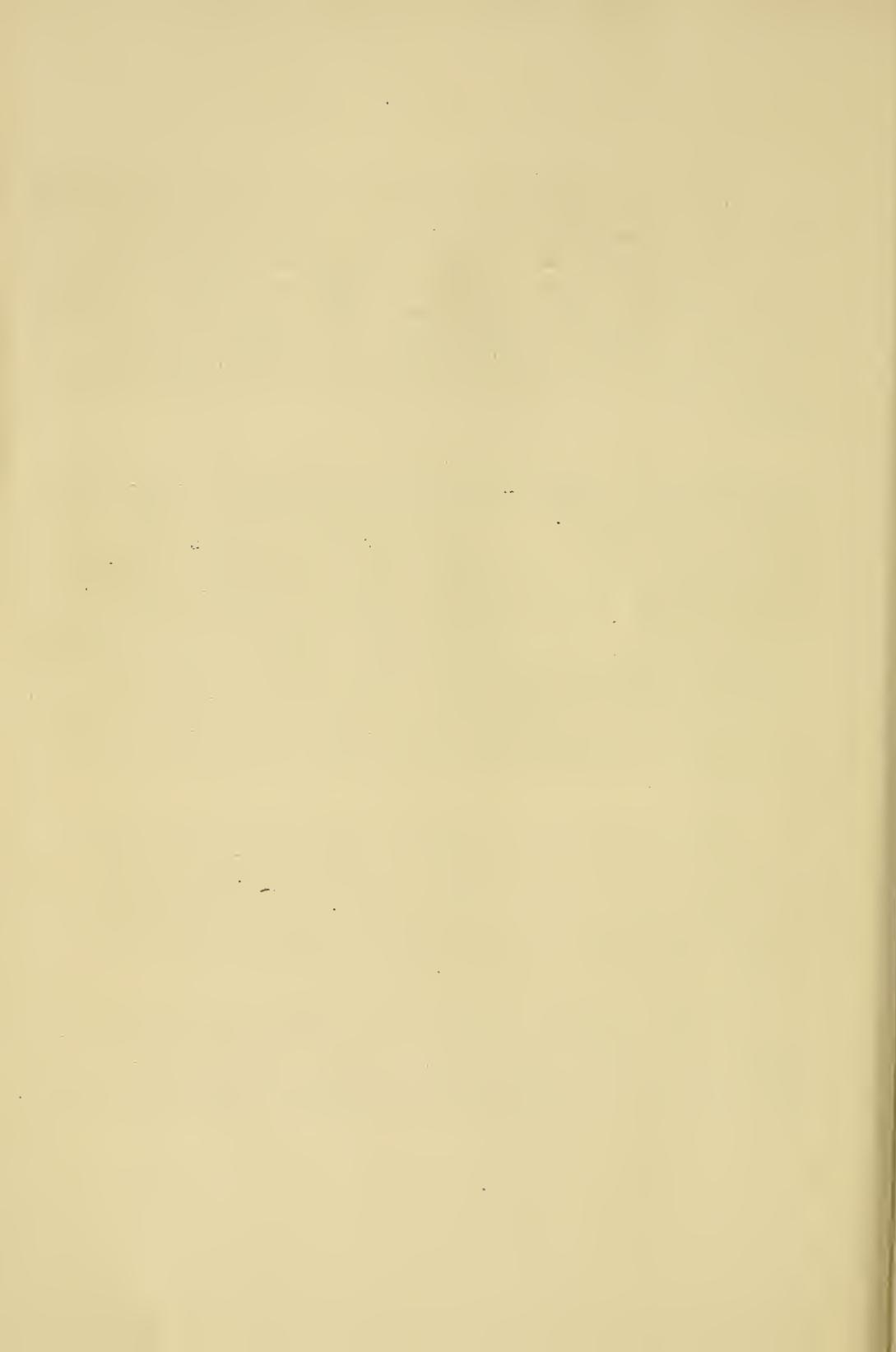


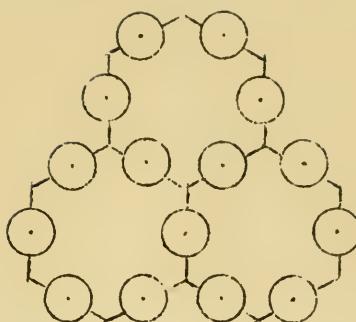
This is probably the type of triple junction which will form most readily in nature, because if more intermediate  $-CH_2-$  groups were introduced they would have too much freedom of movement to produce the triple junction spontaneously. Hydrocarbon chains will not react with each other if they are capable of movement at random in any direction, and that is just the condition which would exist at any point beyond the gamma carbon atom.

If, on the other hand, we omit some of the intermediate  $-CH_2^*$  groups and attempt to form the triple junction at the beta carbon atom, the spirals will have to be brought so close together that there would probably be considerable repulsion between them due to thermal vibration of the atoms. Such a triple junction could probably not form spontaneously unless the spirals were crowded together from the outside, but the presence of substances like iso-leucine and valine among the decomposition products of proteins seems to show that triple junctions of the beta type do occur at times.

The existence of both beta and gamma junctions in the same protein is indicated by the occurrence among protein decomposition products of substances like valyl-leucine which contains a beta junction at one end of the molecule and a gamma junction at the other end.

If we connect together a large number of spirals by means of triple junctions of either the beta or the gamma type, they will form collectively a cluster of hexagonal compartments.

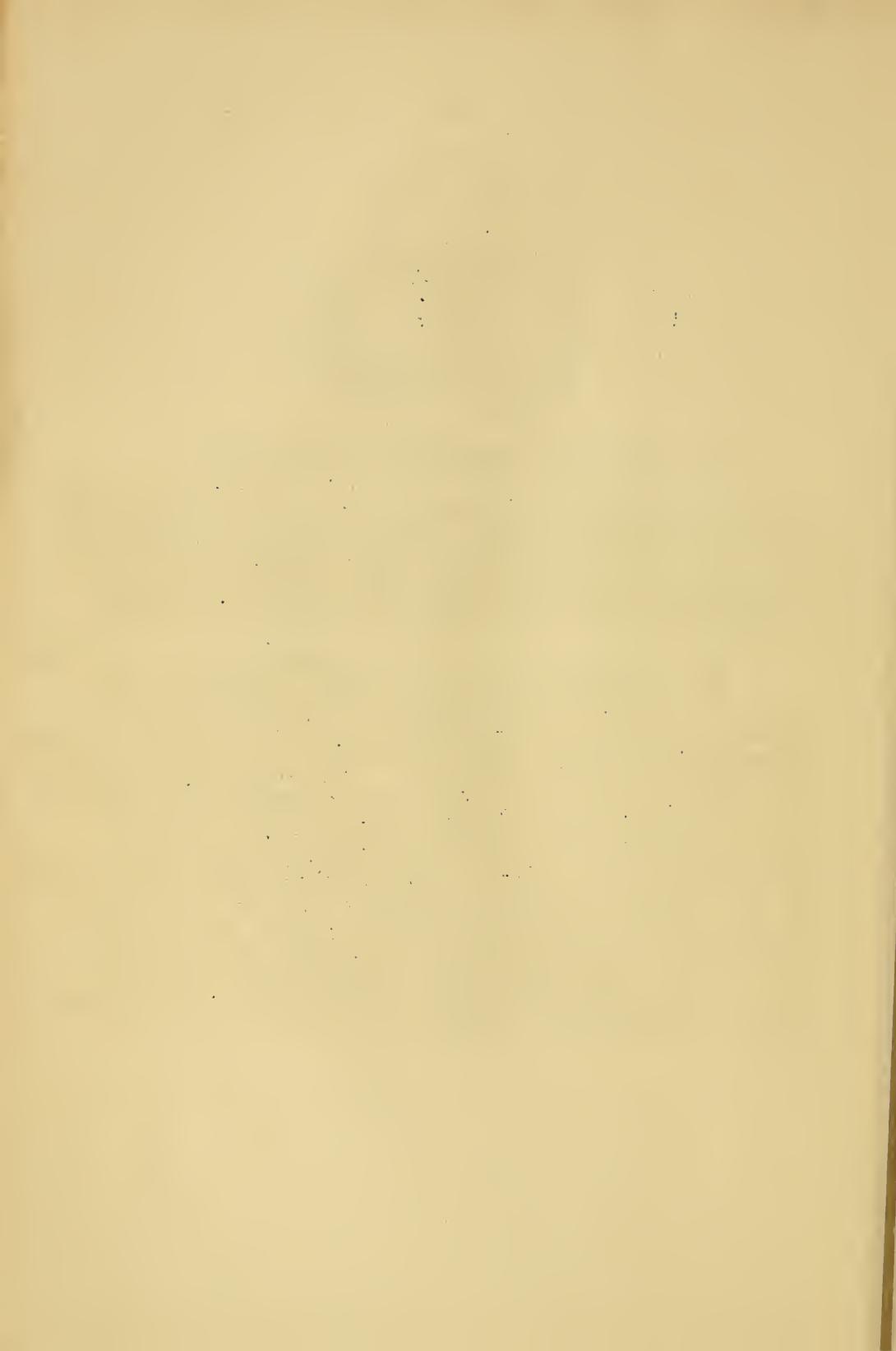


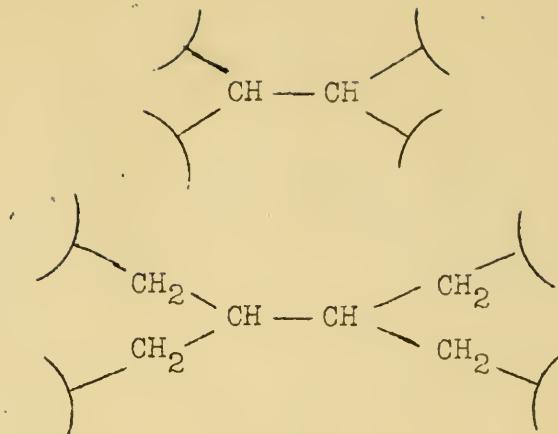


### The cellular structure of proteins.

In living tissues these will be filled with water or dilute salt solution, and it will be observed that the vacant spaces in these compartments have a combined cross-sectional area equal to about three-fourths of the entire area of the figure.

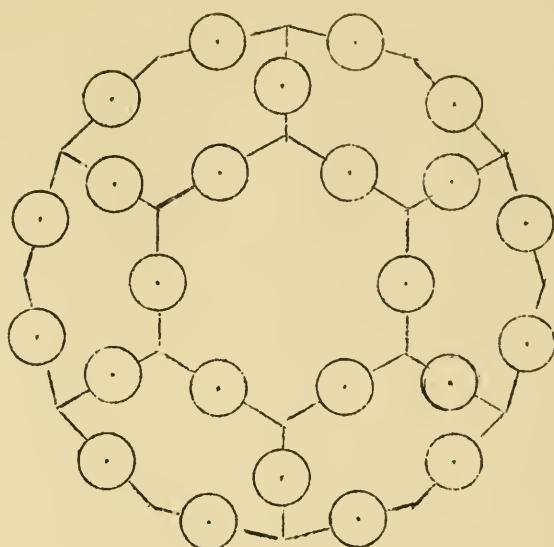
The hexagonal form of compartment is believed to be the form which occurs most frequently in nature, because the hexagon is one of the few figures which when duplicated will completely cover an area of indefinite size. The only other possibilities are quadrilateral and triangular compartments, but as these would require the coupling together of four or six spirals respectively, it is considered highly improbable that they occur to any great extent in nature. It is doubtful whether connecting complexes between six spirals could form spontaneously under any conditions, but connecting complexes between four spirals could probably be formed occasionally as follows:





A cluster of three polypeptide spirals with a complete triple junction at the center ought to possess all the fundamental characteristics of life, provided it is equipped with a stable outer structure. A group of three hexagonal compartments as illustrated on the preceding page could probably not exist in nature because each compartment would have three exposed corners which would render it very vulnerable. Regardless of how many additional compartments we add to this structure, the maximum number of exposed corners can never be less than two. But at the surface of the organism there is really no necessity for confining ourselves to the use of hexagons. If, for example, we form the surface structure of pentagons instead of hexagons, the number of exposed corners on each compartment would be reduced to one, and our organism would appear in cross-section somewhat as follows:





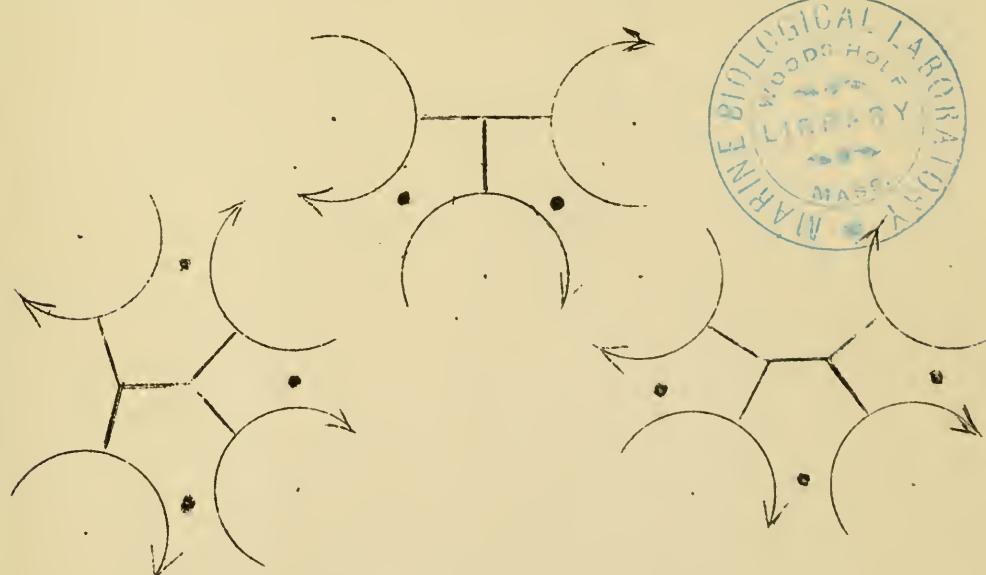
Cross-section of a simple living organism.

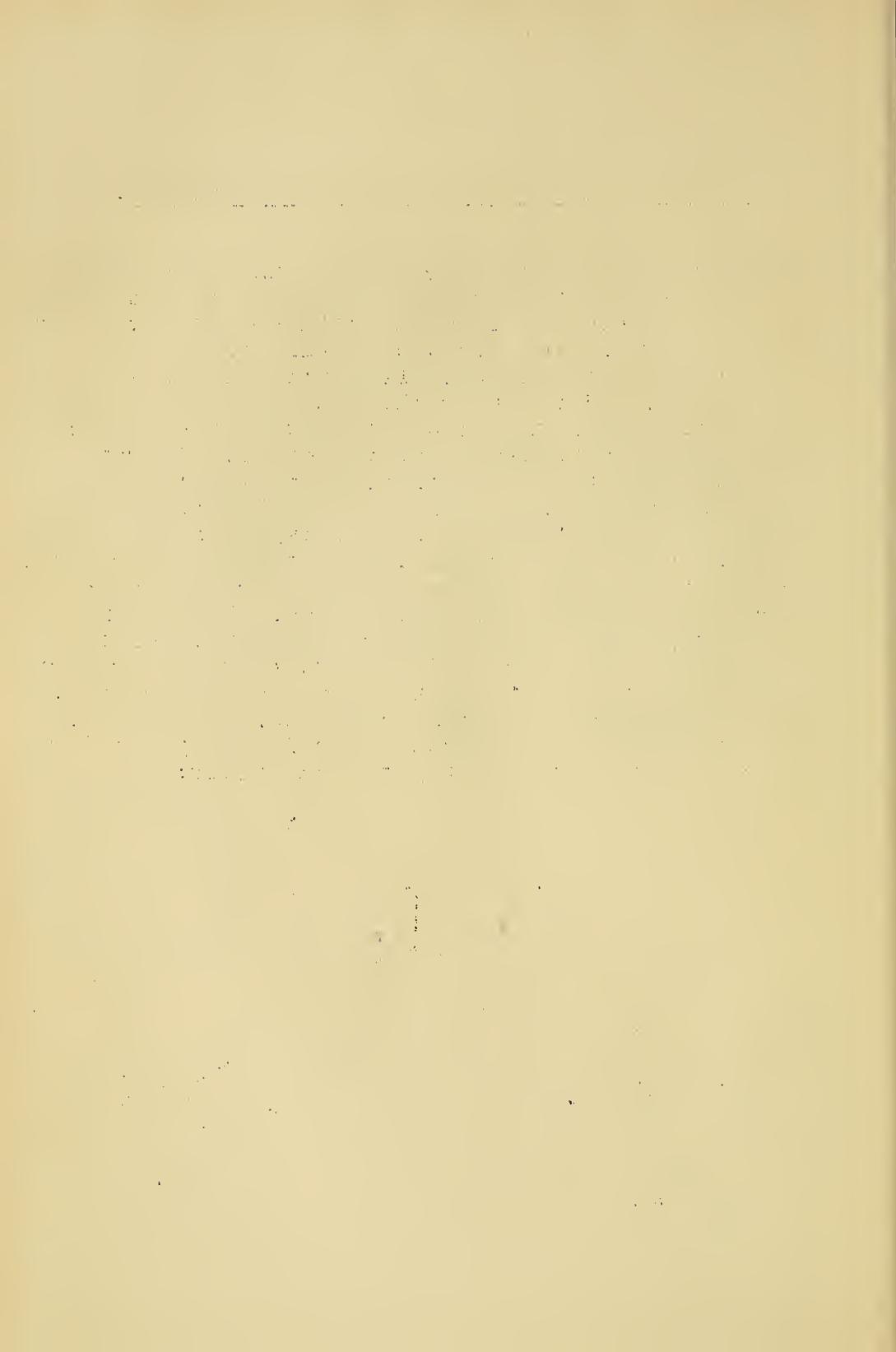
Perhaps cystine, which occurs in small amounts in the decomposition products of all proteins, forms part of this surface structure.



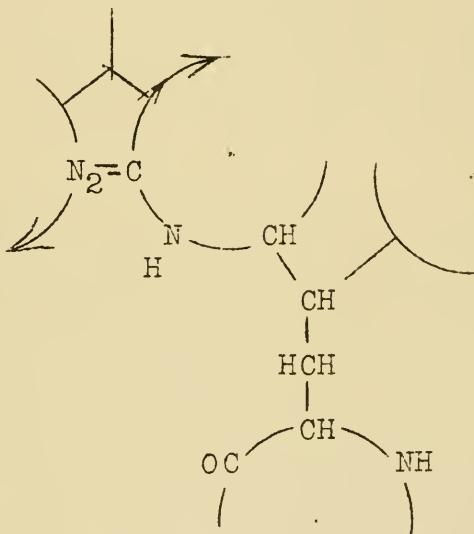
Direct Chemical Union between Spirals.

We have heretofore assumed that connection between adjacent spirals takes place only through the hydrocarbon side chains attached to the alpha carbon atoms. This is undoubtedly the primary mode of connection, but after two spirals are thus connected together there may be a secondary connection between the amino groups of one spiral and the carbonyl groups of the other. If both spirals have the same direction of twist, the amino hydrogen of one spiral will be positioned directly opposite the carbonyl oxygen of the other spiral, so that there will be a tendency for water to split off, leaving the amino nitrogen to combine directly with the carbonyl carbon. In this manner there may be produced either the pyrrole or the pyrimidine ring, depending on whether the primary connection was of the beta or of the gamma type. As shown in the following diagrams, various different configurations can be produced by joining adjacent spirals directly to each other:

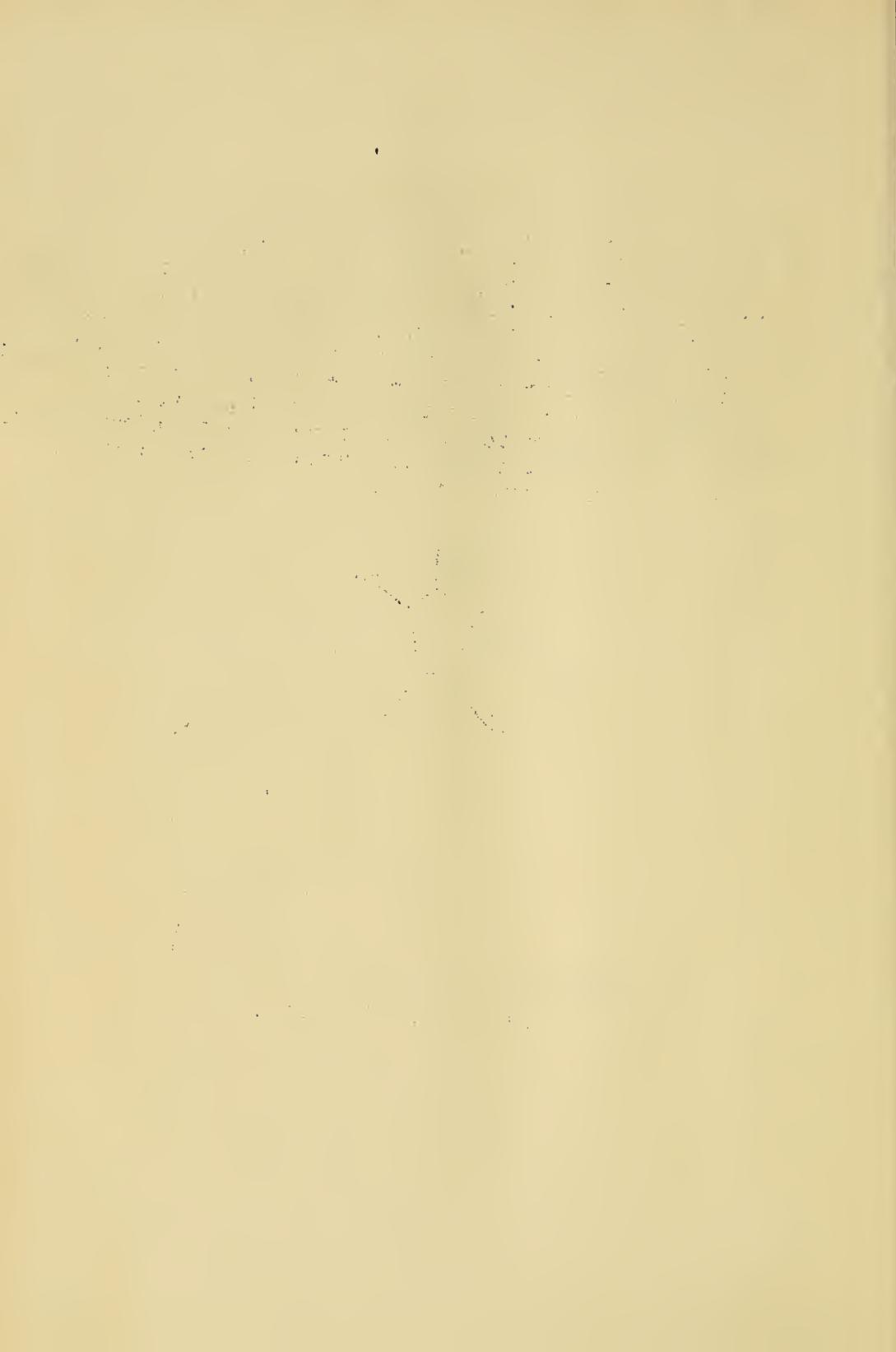




A carbonyl carbon atom should be able to unite in this manner with two nitrogen atoms of an adjacent spiral, and since it is already joined to one nitrogen atom of the same spiral, there will be produced in this manner the guanidine complex which occurs at one end of the arginine molecule. The three intermediate  $\text{CH}_2^*$  groups of the arginine molecule are exactly the number that would occur in passing over to the next adjacent spiral if the intermediate junction is partly of the beta and partly of the gamma type.



Arginine in situ.



Conclusion.

The correctness of the above hypothesis depends in a large measure on whether we were justified in making the assumption that the fundamental life processes are inherent in the molecular structure of the proteins, and are not primarily dependent on any specific physical heterogeneity. This assumption is clearly contrary to orthodox theories which attribute just as much importance to the physical heterogeneity of protoplasm as to the chemical constitution thereof, but the failure of orthodox theories to account for and explain the fundamental life processes should be sufficient justification for attempting the solution of the problem on a new basis.

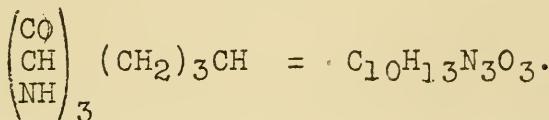
The molecular structure of proteins will probably never be established conclusively by chemical analysis alone. It is, in fact, doubtful whether protein molecules are of uniform size and composition. According to the foregoing hypothesis protein molecules, when dissolved in water or dilute salt solution probably consist of platelets of irregular form and size which have become separated from a cluster of hexagonal compartments. The methods of analytical chemistry can tell us only what the fragments of protein structure are and what the elementary composition thereof is. In order to find out how these fragments were joined together we must take into consideration the principles of biology, although after a certain scheme has been suggested, we may determine the probable correctness thereof by comparing the elementary composition of such hypothetical structure with that found experimentally.



All proteins, (with the exception of protamines and histones,) have approximately the following percentage composition:

Carbon	Hydrogen	Nitrogen	Oxygen	Sulphur
50-55	6.9-7.3	15.0-19.0	19.0-24	0.3-2.4

If we take, as a representative sample of our hypothetical substance, a complete triple junction of the gamma-gamma-gamma type and one-half of each of the three adjacent spirals, then the empirical formula therefor may be derived as follows:



This will give the following percentage composition:

Carbon	Hydrogen	Nitrogen	Oxygen
53.8	5.8	18.8	21.5

The values thus calculated are in fairly accurate agreement with the experimental values, except that the hydrogen is slightly low, but that is just what would be expected because of the difficulty of obtaining proteins in perfectly anhydrous condition. Another possible explanation for the low hydrogen percentage is that the protein molecule in water solution may consist of only a thin sheet taken transversely of the axes of the spirals, so that many additional hydrogen atoms or hydroxyl groups will be required for combination with the free ends of the spirals. For example, if we include only two additional hydrogen atoms in our theoretical formula, the percentage of hydrogen will be brought up to the values obtained experimentally.



If we assume the triple junction to be only two-thirds gamma and one-third beta, then the percentage composition will be as follows:

Carbon	Hydrogen	Nitrogen	Oxygen
52.1	5.2	20.1	23.1

Instead of dealing with absolute percentages of the various elements, it is better to deal with ratios of carbon to nitrogen, because the ratio of these two values will be unaffected by varying amounts of water that may be present, or by the extra hydrogen that may be attached to the free ends of the spirals.

From the above theoretical data we obtain the following ratios of carbon to nitrogen:

With triple junctions of the  
gamma-gamma-gamma type, 2.86

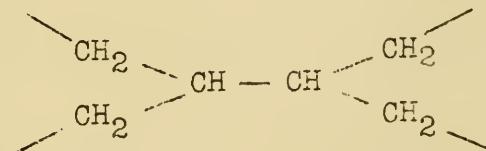
With triple junctions of the  
beta-gamma-gamma type, 2.59

With quadruple junctions  
of the type:



2.14

With quadruple junctions  
of the type:



3.00



No attempt has been made hereinabove to explain the chromosome mechanism in detail. Chromosomes do not occur in the simplest organisms such as the bacteria, but appear to be the first stage in evolution to higher types, whereas the purpose of the present treatise is to explain life processes only in so far as they are of universal occurrence and common to all forms of life.

Carl F. Krafft.







